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APPLICATION FOR UNITED STATES LETTERS PATENT
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Attorney Docket No. 004367.00005)

Title: Paramagnetic Polymerized Protein Microspheres
And Methods of Preparation Thereof

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PARAMAGNETIC POLYMERIZED PROTEIN MICROSPHERES AND METHODS OF PREPARATION THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is based on, and claims the benefit of, co-pending United States Provisional Application Serial No. 60/300,943, filed on June 26, 2001, and entitled "Paramagnetic Polymerized Protein Microspheres" which is incorporated herein by reference.

BACKGROUND OF THE INVENTION

1. FIELD OF THE INVENTION

The invention relates to contrast agents and methods of preparation thereof for use in various imaging modalities, and/or for use in therapy.

2. DESCRIPTION OF RELATED ART

Introduction to Imaging Modalities

Various *in vivo* imaging processes, including ultrasound, magnetic resonance and computed tomography, are used as medical diagnostic tools. The underlying principle of each imaging modality is generally that the differences in a particular property or properties (e.g., acoustic properties, proton density, etc.) of the organs, tissue and other substances within the body at a location to be examined are detected and then translated into an image. The various modalities, however, rely on very different principles to generate images. The effectiveness of any of these imaging processes, and the resolution of the resulting images, in a great part depends on the degree of contrast between the body parts that the imaging equipment is able to detect so as to delineate the features of the region of interest within the subject body area. As a result, use of internally administered agents specifically designed to

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enhance the degree of contrast detected with a particular modality has become common. The differences in the imaging techniques involved with various modalities, however, have thus far generally restricted the use of any particular contrast agent to one imaging modality.

Ultrasound

Ultrasound ("US") is an imaging process that relies on the reflection of sound waves within the body to produce an image thereof. High frequency sound (ultrasonic) waves, which are above the range of sound audible to humans, are directed at the region of interest within the body. The waves are reflected back wherever there is a change in the physical parameters of the structures within the body, e.g., a change in density between two adjacent organs. The ultrasound equipment receives the reflected sound waves and transmits them into an image based on the differing levels of intensity of the reflected waves.

Use of a contrast agent enhances the differences in intensities of the reflected waves. For example, intravenous encapsulated microbubble contrast agents have become an established clinical tool for enhancing medical diagnostic ultrasound and Doppler sensitivity. Some current contrast agents function to enhance the appearance of the blood pool and to define its architecture and integrity. Other contrast agents provide passive, targeted, organ-specific imaging based upon the biodistribution and pharmacokinetics of the circulating contrast agent, localizing in, for example, the liver, spleen, kidney and lung.

The interaction of encapsulated microbubble contrast agents with ultrasound is complex. The microbubble response relative to a driving acoustic pressure can be divided into three categories: (1) linear scattering, (2) nonlinear scattering, and (3) cavitation/destruction. Microbubbles produce linear scattering with low acoustic driving

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